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EXAMINER

BEISNER, WILLIAM H

ART UNIT PAPER NUMBER

1744

DATE MAILED: 07/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/003,481

Applicant(s)

VELLINGER ET AL.

Examiner

William H. Beisner

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 22 April 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 4-36 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 4-36 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/22/05 has been entered.

### ***Claim Objections***

2. Claims 8-17, 19, 20 and 24 are objected to because of the following informalities: Claims 8-17, 19, 20 and 24 as written depend from cancelled claim 3. It appears that these claims should depend from new independent claim 4 and will be examined on their merits as though these claims depend from claim 4. Additionally claim 17 is incomplete and does not end with a period. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 4-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not

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described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

With respect to new claim 4, this claim recites that the apparatus includes both “a sealed compartment for sample-collection bags providing a level of chemical containment for safety” and “a rotary sample collector in fluid communication with said reactor vessel”. However, the originally filed disclosure only provides support for an apparatus that includes either of the listed sample collection structures. Nothing in the originally filed disclosure would have conveyed to one of ordinary skill in the art that applicants’ invention at the time of filing the application encompassed a device that included both sampling structures in the same device. See pages 11-12 which discuss sample-collection system (30) and pages 17-19 which discuss sample collection system of Figure 12 which is different from that of system (30). Nothing in the originally filed disclosure conveys to one of ordinary skill in the art that the invention included the use of both sampling devices in the same system.

With respect to claimed “means for controlling the humidity within said reactor vessel”, while the originally filed disclosure provides support for controlling the humidity within a housing enclosing the reactor vessel, the originally filed disclosure fails to provide support for “means for controlling the humidity within said **reactor vessel**” (See page 13, lines 4-12).

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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6. Claims 4-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 4, the recited electrical power source is indefinite because the claim fails to provide structural cooperation between the power source and the rest of the positively recited elements of the device. The “said upper collector plate” and “said lower collector plate” lack antecedent basis. These appear to be structures that are associated with the “rotary sample collector”. If a single chamber defines the reactor, how the different outlets provide just medium and cells w/medium as recited in the claim? The recited means for collecting fluid and cell samples is indefinite because it is not clear how this structure cooperates with the rest of the positively recited elements of the device. Also, how does this structure differ from the “sealed compartment for sample-collection” and “rotary sample collector” recited in the claim? Furthermore, the recited “computer program” is indefinite because while the claim recites a list of intended functions to be performed by the system, the language fails to positively recite which previously positively recited structural elements are controlled by the program so as to provide the intended steps. Finally, with respect to the rotary sample collector, mere recitation of “a rotary multiple sample collector” linked with its intended use is not enough to clearly define the metes and bounds of the structure of the device encompassed by this claim language. Note, this claim language is not considered to be covered by 35 USC 112, sixth paragraph. While the language recites the intended function of the sample collector, it is not clear what structures provide the intended functions and/or how the collector and/or associated structure cooperate with the rest of the positively recited device.

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Claims 5-7 and 14 are indefinite for the same reasons as discussed above with respect to the “rotary sample collector”.

Claim 8 is indefinite because the claim language fails to positively set forth structural cooperation between the recited “connection means” and the rest of the positively recited structures that define the device.

Claim 9 is indefinite because “said means for exchanging gases” lacks antecedent basis. Note claim 4 does not recite this structure as part of the device.

Claim 10 is indefinite because it fails to recite how the recited filter is provided in the reactor vessel and/or structurally cooperates with the two different outlets.

Claim 11 is indefinite because “said peristaltic pump” lacks antecedent basis. Claim 4 fails to recite a “peristaltic pump”. Also, the claim fails to positively recite how the bag and/or pump structurally cooperate with the recited elements of claim 4 so as to provide the required medium feeding.

Claim 17 is indefinite because it is not clear how the claim further defines the structure of the device of claim 4.

Claim 19 is indefinite because the claim is limited to a method while the claim depends from an apparatus-type claim. Is a method or apparatus being claimed in this claim?

Claim 20 is indefinite because while it recites that the device further includes a video device and microscope system, the claim fails to positively set forth structural cooperation between these new elements and the rest of the positively recited structural elements that define the claimed device.

Claim 21 is indefinite because “the observation cell” lacks antecedent basis.

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Claim 23 is indefinite because while it recites that the device further includes a modular slide system, the claim fails to positively set forth structural cooperation between this new element and the rest of the positively recited structural elements that device the claimed device.

Independent claims 26 and 27 are indefinite for the same reasons as set forth with respect to claim 4.

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

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invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 4, 5, 8-12, 15-19, 27-30 and 33-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knazek et al.(WO 90/02171) in view of Goffe (US 5,882,918).

The reference of Knazek et al. discloses a bioreactor apparatus that includes a cylindrical reactor vessel (11) that includes two cover plates, fill ports (13a, 13b, 15a, 15b) and a polymeric filter (12) (See page 21, lines 4-14). The apparatus includes a length of permeable tubing (18) and a pump (24), a fresh medium storage container (150), a sample collection container (160) that includes pinch valves (See page 13, lines 6-20). The device when used in an incubator device includes a device for controlling humidity (See page 18, lines 19-28) and is sealed within the external housing of the incubator device. The apparatus also includes a controller (80) with an electrical power source located outside the incubator enclosure (See page 19, lines 28-34). With respect to the claimed "rotary sample collector", in the absence of further positively recited, sample collection chamber (160) is considered to meet this claim language since it includes a cap (161) that can be rotated.

Claim 4 first differs by reciting that the reactor vessel includes rotary unions.

The reference of Goffe discloses that it is known in the art to rotate a hollow fiber reaction vessel that is held within an incubation enclosure by rotating the vessel (See column 5, lines 15-49).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to rotate the vessel of the primary reference so as to agitate the vessel as suggested by the reference



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of Goffe. When employing complete 360 degree rotation as suggested by Goffe, it would have been obvious to provide the vessel with rotary unions for the known and expected result of allowing the medium to communicate with the vessel during the rotation of the vessel.

Note the controller of the system of the primary reference is capable of being programmed in view of the use of a microprocessor to control the system (See page 26, lines 14-34).

With respect to the claimed use of a bag rather than a bottle as a container for the medium, the primary reference recognizes that other known culture containers can be used in place of the disclosed bottles (See page 26, lines 27-33). As a result, it would have been obvious to one of ordinary skill in the art to employ a bag rather than a bottle for the known and expected result of providing an alternative means recognized in the art to achieve the same result.

With respect to claim 5, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide a plurality of sample collection vessels (160) so as to provide a means recognized in the art for collecting a plurality of samples over time during the culture process.

With respect to claim 8, the reference of Knazek et al. discloses fluid connection means (136).

With respect to claim 9, the reference of Knazek et al. discloses the use of permeable tubing (18) and a pump (24). With respect to the use of peristaltic pumps, while the primary reference is silent as to the use of these pumps, in the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art to employ peristaltic pumps within the system of the primary reference for the known and expected result

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of providing an art recognized means for flowing media within a culture system while minimizing the contact of the media with the pumping device.

With respect to claim 10, in the absence of further positively recited structure, the filter of the reference of Knazek et al. is considered to meet the claim limitation "low pressure drop" since the device is capable of removing just medium and/or medium and cells from the different outlet ports of the device.

With respect to claim 11 and use of a bag rather than a bottle as a container for the medium, the primary reference recognizes that other known culture containers can be used in place of the disclosed bottles (See page 26, lines 27-33). As a result, it would have been obvious to one of ordinary skill in the art to employ a bag rather than a bottle for the known and expected result of providing an alternative means recognized in the art to achieve the same result.

With respect to claim 12, when using a plurality of sample collectors as suggested above, it would have been obvious to one of ordinary skill in the art to provide manifolding and valves for controlling the flow of medium to the plurality of collection bags.

With respect to claim 15, the permeable tubing (18) of Knazek et al. provides oxygenation of the medium within the reactor vessel.

With respect to claim 16, the use of pH, glucose and oxygen sensors with bioreactors is notoriously well known in the art and would have been obvious for the known and expected result of maintaining culture conditions that ensure efficient culturing conditions and cell viability.

With respect to claim 17, this claim is of the same scope as claim 4.

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With respect to claim 18, the reference of Knazek et al. discloses the use of a polymeric filter (12) (See page 21, lines 4-14).

With respect to claim 19, statements of intended use carry no patentable weight in apparatus-type claims.

With respect to claim 27, the permeable tubing (18) of Knazek et al. provides oxygenation of the medium within the reactor vessel.

With respect to claim 28, see the discussion of claim 4 above.

With respect to claims 29 and 30 and the use of peristaltic pumps and pinch valves, while the primary reference is silent as to the use of these pumps, in the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art to employ peristaltic pumps within the system of the primary reference for the known and expected result of providing an art recognized means for flowing media within a culture system while minimizing the contact of the media with the pumping device.

With respect to claim 33, the use of pH, glucose and oxygen sensors with bioreactors is notoriously well known in the art and would have been obvious for the known and expected result of maintaining culture conditions that ensure efficient culturing conditions and cell viability.

With respect to claim 34, the controller of the system of the primary reference is capable of being programmed in view of the use of a microprocessor to control the system (See page 26, lines 14-34).

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With respect to claim 35, in the absence of further positively recited structure, the device of the modified primary reference is capable of being used and/or functioning in low gravity environment.

11. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Knazek et al.(WO 90/02171) in view of Goffe (US 5,882,918) taken further in view of Pickering (US 4,161,172).

The combination of the references of Knazek et al. and Goffe has been discussed above.

While the primary reference discusses the use of a humidity control device, the reference is silent as to the structure of the device.

The reference of Pickering discloses that it is known in the art to provide an incubator device with a humidifier that includes a water-saturated sponge (See column 11, lines 47-51).

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide the incubator of the primary reference with a humidifier as disclosed by the reference of Pickering for the known and expected result of providing a means recognized in the art for stabilizing the humidity within an incubator device.

12. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Knazek et al.(WO 90/02171) in view of Goffe (US 5,882,918) taken further in view of Schwarz et al.(US 5,437,998) and Greenberger et al.(US 6,008,010).

The combination of the references of Knazek et al. and Goffe has been discussed above.

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Claim 20 differs by reciting that the system includes a video device and microscope system.

The reference of Schwarz et al. discloses that it is known in the art to monitor the contents of a rotating bioreactor with a viewport (50) for microscopic observation (See column 8, lines 30-32).

The reference of Greenberger et al. discloses that it is known in the art when microscopically monitoring a cell culture, it is known to employ a video device (See cell monitoring system (300)).

In view of these teachings, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide the system of the modified primary reference with a cell monitoring system as suggested by the references of Schwarz et al. and Greenberger et al. for the known and expected result of providing a means recognized in the art for determining the state of the cells that can be used for maintaining desired culture conditions within the culture vessel.

13. Claims 21-26 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knazek et al.(WO 90/02171) in view of Goffe (US 5,882,918); Schwarz et al.(US 5,437,998) and Greenberger et al.(US 6,008,010) taken further in view of Akashi (JP 03-160980).

The combination of the references of Knazek et al., Goffe, Schwarz et al. and Greenberger et al. has been discussed above.

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The above claims first differ by reciting that the culture system further includes a microscopic observation path in the flow line for monitoring the cell sample in the culture system.

The reference of Akashi discloses that is it well known in the art to optically monitor a culture system using a microscopic observation flow cell or slide (19, 4a).

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide the flow line of the modified primary reference with a monitoring system as suggested by the reference of Akashi for the known and expected results of monitoring the culture system for contamination as suggested by the reference of Akashi.

With respect to the use of a dual optical path system, in the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ optical paths that allow a single camera to be employed to monitor both optical view areas of the system for the known and expected result of reducing costs of the system by only requiring the use of a single video device to monitor both viewing areas of the system.

With respect to the claimed fields of view, in the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art to determine the optimal fields of view based merely on the size of the culture system and/or the size of the cells being cultured while providing the level of monitoring required to monitor the state of the cells and/or contamination within the culture system.

The video device and flow system are structurally capable of providing still frames and/or stopping the flow of medium.

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With respect to the use of LEDs, it would have been obvious to one of ordinary skill in the art to provide lighting devices for optically monitoring the system as suggested above. The use of LEDs would have been obvious for the known and expected result of providing a means known in the art for providing illumination without generating large amounts of heat and/or providing a light source that is economical and last longer than conventional light bulbs.

14. Claims 31 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knazek et al. (WO 90/02171) in view of Goffe (US 5,882,918) taken further in view of Kearney (US 5,424,209).

The combination of the references of Knazek et al. and Goffe has been discussed above.

With respect to the levels of containment recited in claims 31 and 32 above, the reference of Kearney discloses that it is known in the art to provide at least three levels of containment with respect to a self-contained culture system (See the abstract).

As a result, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide levels of containment within the system of the primary reference for the known and expected result of isolating the cells and medium from the ambient surroundings.

***Allowable Subject Matter***

15. Claims 6, 7 and 14 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, first and second paragraph, set forth in this Office action.

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16. The following is a statement of reasons for the indication of allowable subject matter: Claims 6, 7 and 14 would be allowable because the prior art of record fails to teach or fairly suggest the combination of the elements recited in these claims with a sampling system as recited in claims 6, 7 and 14 wherein the sampling system includes a plurality of sample retaining chambers and filters with a rotary inlet port and wherein the sampling system is capable of collecting cells on the filter, fixing the cells and storing the cells.

#### ***Response to Arguments***

17. Applicant's arguments with respect to the pending claims have been considered but are moot in view of the new ground(s) of rejection.

#### ***Conclusion***


18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to William H. Beisner whose telephone number is 571-272-1269. The examiner can normally be reached on Tues. to Fri. and alt. Mon. from 6:15am to 3:45pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Kim can be reached on 571-272-1142. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.



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William H. Beisner  
Primary Examiner  
Art Unit 1744

WHB